

Drugs, Dangers and Directions

Pages with reference to book, From 81 To 84

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These questions were received and answered by the Drug Information Centre, recently set up at the Khyber Medical College, Peshawar, by the Department of Pharmacology and Therapeutics.

Question

Phony! hydrargyri borass. (DCL). Trade Name Exemycol Gel.

If this preparation is used on skin for about 4-6 weeks, will it produce harmful systemic effects?

Ahmad Iqbal

Khyber Medical College Peshawar.

Answer

The organic mercury compounds are chiefly used as antiseptic applications to the skin and mucous membrane. A lotion containing 1 in 3000 to 1 in 1,500 phenylmercuric nitrate is used for disinfection of the skin and application to wounds. Some organic mercury compounds are less toxic than the inorganic salts and are somewhat more antibacterial.

Exomycol (Phenyl hydrargyri borass) Gel. & S. Afri. Phenylmercuric borate has similar actions as Phenylmercuric Nitrate. "An 18 months old girl developed glycosuria, albuminuria, aminoaciduria and impaired phosphate reabsorption following the application of a glycerinated solution of Phenylmercuric borate to her gums for a period of one year.

Its solution in soap was absorbed through the skin, metabolite are excreted in the urine as inorganic mercury which lead to kidney damage.

In view of the above observations it can be inferred that nephrotoxicity from this preparation after 4-6 weeks of topical application is less probable.

Allergic reactions may be induced and contact allergies, even asthma have been traced to phenylmercuric' compounds.

Gells:

Gels are semisolid or solid preparations made with the aid of a suitable gelling agent such as gelatin, tragacanth, gelatinised starch carbomer, or a cellulose derivative.

Aqueous gels are especially useful for the treatment of the scalp or skin' where a non greasy preparations is required.

Ointments:

'Ointments are semisolid preparations for external application. They consist usually of a drugs incorporated in fatty, waxy or synthetic bases.

Question

How much is Rifampicin effective in the treatment of Tuberculous Meningitis. Does it cross the Blood Brain Barrier in sufficient amounts to be effective?

Nasser Uddin Azam Khan

Med. "A" Unit, Khyber Hospital, Peshawar.

Answer

Rifampicin is distributed through out the body and is detectable in many organs and body fluids including, CSF.

Rifampicin is active orally, penetrates well into the cerebrospinal fluid and is thus of use in the treatment of Tuberculous Meningitis. Due to its excellent penetration in CSF it can be considered as an

ideal companion drug to Isoniazid for the treatment of patients with Tuberculous Meningitis.

Rifampicin is a drug of choice for Chemoprophylaxis of meningeal disease in household contact of patients with such infections.

Rifampicin is the most important drug in the therapy of Tuberculous Meningitis which approaches activity of Isoniazid. In Meningeal Tuberculosis it is essential to use Isoniazid which penetrates well into the CSF. Of the alternative drugs rifampicin ethionamide and cycloserine readily enter the CSF from blood.

In the treatment of Tuberculous Meningitis, therapy should always include Isoniazid with either rifampicin or Streptomycin, probably the former.

Question

Why does Phenobarbitone causes convulsions in some patients?

Mohammad Israel

Distt. Hospital, Mardan.

Answer

Drowsiness is the most common adverse effect, although some children may become hyperactive. This paradoxical response is particularly common in children with brain damage. Elderly persons may exhibit idiosyncratic excitement instead of depression following the use of barbiturates. Barbiturates antagonise analgesics and are inappropriate for the treatment of pain from any cause. Hence, excitement, delirium and restlessness may be produced, particularly in patients who experience uncontrolled Pain.

Allergic reactions occur occasionally with Phenobarbitone and rashes, restlessness and excitement may be seen, but an agreed upon explanation is lacking. However, the following have been observed :-

1. Phenobarbitone is strictly contraindicated in porphyrias, since production of severe toxic effects such as paralysis may occur because, Phenobarbitone stimulates the liver Parenchymal cells to form an enzyme (Amino Levulinic acid synthetase). This enzyme controls the formation of Porphyrin by condensation of co-enzyme A with glycine to form amino-levulinic acid.
2. Low plasma and CSF levels of folate and megaloblastic anaemia have often been reported after prolonged administration of Phenobarbitone, Phenytoin, Primidone and Phenobarbitone or their combinations, which might be due to induction of hydromylation systems in the Liver by these drugs, resulting in increased utilization of folate.
3. Folic acid administration in Anaemic epileptic patients improve the mental state of confused epileptics but may cause an increase in the frequency of fits although some workers disagree with these findings.
4. Hypocalcaemia and elevations of serum alkaline Phosphatase levels in 15% of epileptic patients treated with anti-convulsants have been observed. Anticonvulsants include liver microsomal enzymes to cause vit. D deficiency by increased breakdown of vit. D, low bone alkaline Phosphatase levels and many of whom also have a degree of hypocalcaemia.

Question

Metoclopramide (Maxolon) caused convulsions in three patients. Is there any reference to its occurrence. How much is it common.

Resident Medical Office,

Kh yber Teaching Hospital, Peshawar.

Answer

This drug is structurally very similar to procainamide, in fact its derivative and interestingly enough it stimulates gastric motility and relaxes the pylorus, so stomach emptying is speeded. It stimulates

prolactin secretion. These properties may contribute to the antiemetic effect and are also used to facilitate intubation procedure, radiological examination of gut, empty the stomach before emergency anaesthesia and in labour.

This drug causes extrapyramidal reactions, even though it is not a phenothiazine. The mechanism by which it causes this syndrome is not known. However these reactions are less common, than with phenothiazine or butyrophenes. Therefore, Metoclopramide should not be given with a phenothiazine since the former drug enhances the extrapyramidal effects of the later.

In a survey reports of 1023 patients and another in 778 patients the incidence of extra pyramidal effect was 1% and nil respectively.

Dystonic reactions to drugs such as metoclopramide are seen almost exclusively in children of the age under 15 years and more commonly females than males. The dyskinesia usually begins within 36 hours and includes trismus, torticollis, facial spasms, opisthotonus and oculogyric crises which disappear within a day of stopping metoclopramide and responded to antiparkinsonian drugs such as peroral benzotropine or Diazepam.

However the fact that five cases of Tardive Dyskinesia in connection with metoclopramide have been reported in the past year is more serious. All patients were women past middle age and had used the drug over prolonged period ranging from four months to many years. Tardive syndrome is a serious neurological disorder characterized by involuntary movements often involving tongue and mouth but involuntary grimaces are also common (Boege Lingual masticatory syndrome). Involuntary movements similar to chorea can also engage extremities and trunk. These symptoms have not disappeared after discontinuing the drug for more than three months.

A medical student took metoclopramide, Seven hours later he developed stretching of the neck muscles and his head was tilted to one side, relieved by I/V Diazepam.

In future it would be valuable to take plasma for estimation of metoclopramide to establish whether the extra pyramidal disturbance is associated with abnormally high blood concentration in relation to the administered dose.

Question

Is there an antidote for poisoning by the most common pesticide used by mothers for delousing their children?

Mehr TajRog/iani

Paediatric Department, Khyber Hospital, Peshawar.

Answer

The specific antidote for the common organophosphate pesticides (parathion, Malathion, Mevinphos and Diazinon) is PROLIDOXIME Chloride (PROTOPAM CHLORIDE, YERST Labs. Division of American Home Products Corporation).

Description

Protopam Chloride is a cholinesterase reactivator, and has the generic name Pralidoxime Chloride. It has also been referred to as 2-PAM Chloride and PAS.

Warning

Use of Protopam should always be under supervision of a Physician.

Treatment

Treatment consists of the following: The most common route of entry in accidental poisoning is by the skin treatment may begin with removal of contaminated clothes and washing of exposed skin with Sodium bicarbonate Solution or alcohol.

There should be maintenance of patient airway and if necessary artificial ventilation may be done.

Antidotes

Atropine has to be given to block the actions of acetyl choline before Protopam reactivates

Cholinesterase.

In the absence of cyanosis, atropine should be given intravenously in doses of 2-4 mg, where cyanosis is present this dose of atropine should be given intramuscularly while simultaneously improving ventilation atropine administration should be repeated at 5-10 minute intervals until sign of atropine toxicity appear. Some degree of atropinisation should be maintained for at least 48 hours. In most instances as much as 100 mg of atropine can be given.

Antidote

Protopam administration should be started at the same time as atropine.

For Adults:- Inject an initial dose of 1-2 gm of Protopam preferably as an infusion in 100 ml of saline, over a 15-30 minutes period. If this is not practicable or if pulmonary oedema is present the dose should be given slowly by intravenous injection as a 5% solution in water over not less than 5 minutes. After about an hour, a second dose of 1-2 gm will be indicated if muscle weakness has not been relieved.

For Children :-The dose should be 20-40 mg per kg., body weight. Treatment will be most effective if given within a few hours after poisoning.

In severe cases, it may be desirable to monitor the effects of the therapy electrocardiographically because of the possibility of heart block due to the anti-cholinesterase.

If poison is ingested it is likely to continue absorption from lower bowel. In such cases additional doses of protopam may be needed every 3-8 hours.

In the absence of severe gastrointestinal symptoms, resulting from the anti-Cholinesterase intoxication, protopam may be administered orally in doses of 1-2 gm (2-6 tablets) every 5 hours. As in all cases of organophosphate poisoning, care should be taken to keep the patient under observation for at least 24 hours.

If convulsions interfere with respiration, sodium thiopentone (2.5% Solution) may be given intravenously with care because barbiturates are potentiated in organophosphate poisoning.

Anticholinesterase Overdosage

As an antagonist to such anticholinesterases as neostigmine, Pridostigmine, and ambenonium, which are used in the treatment of myasthenia gravis. Protopam may be given in a dosage of 1-2g intravenously followed by increments of 250 mg every five minutes.

Precautions

Intravenous administration of Protopam should be carried out slowly and preferably, by infusion, since certain side effects, such as tachycardia, Laryngospasm and muscle rigidity, have been attributed in a few cases to a too rapid rate of Injection, because Protopam is excreted in the urine. Thus dosage should be reduced in the presence of renal insufficiency.

Protopam should be used with great caution in treating organophosphate overdosage in cases of myasthenia gravis since(it may precipitate a myastheric crisis. Since barbiturates are potentiated by the anticholinesterases, they should be used cautiously in the treatment of convulsions; theophylline, aminophylline, succinylcholine reserphine, and Phenothizine-type tranquilizers should be avoided in patient, with organophosphate poisoning.

Adverse Reactions

Dizziness, blurred vision, diplopia and impaired accommodation headache, drowsiness, nausea, tachycardia, hyperventilation, and muscular weakness have been reported after use of Protopam but it is very difficult to differentiate the toxic effects produced by atropine or the organophosphate compounds from those of the drug. When atropine and Protopam are used together, the signs of atropinization may occur earlier than might be expected when atropine is used alone.

Over Dosage

Artificial respiration and other supportive therapy should be administered as needed.

How Supplied

One 20 ml vial of 1 gm of sterile Protopam Chloride (Pralidoxime Chloride) while to off white porous

cake; one 20 ml ampul of sterile water for Injection; sterile disposalbe 20 ml syringe needle alcohol swab This is a single dose kit for intravenous administration.